**WHAT IS CLAIMED IS:**

1. A method of preparing a DNA molecule having an amplifiable region comprising:
   a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;
   b) attaching upstream adaptor molecules to ends of DNA molecules of the sample to provide a nick translation initiation site;
   c) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5'-3' exonuclease activity to produce nick translate molecules;
   d) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

2. The method of claim 1, wherein the ends of said DNA molecules are produced prior to the attachment of said upstream adaptor molecule.

3. The method of claim 2, wherein the ends of said DNA molecules are produced by at least one restriction enzyme, by an endonuclease, by mechanical shearing, by a chemical, or a combination thereof.

4. The method of claim 1, wherein said DNA polymerization step incorporates at least one modified nucleotide into said nick translate molecule.

5. The method of claim 4, wherein said modified nucleotide is an exonuclease-resistant nucleotide.

6. The method of claim 1, wherein said adaptor attached nick translate molecules are separated.

7. The method of claim 6, wherein said separation is based upon size.

8. The method of claim 1, wherein said adaptor attached DNA molecule is denatured

9. The method of claim 8, wherein the denatured DNA is separated.

10. The method of claim 1, wherein a single stranded nick translation product is separated from the DNA sample template strand.

11. The method of claim 1, wherein said DNA is subjected to nick translation for a specified period of time.

12. The method of claim 11, wherein the nick translation product has a predictable length.

13. The method of claim 11, wherein the nick translate molecules are substantially similar in size.

14. The method of claim 1, wherein the upstream adaptor comprises a nick translation initiation site.

15. The method of claim 1, wherein the upstream adaptor further comprises a primer binding region, a hybridization domain, a ligation domain, a detection domain, an amplification domain, a recombination domain, or a combination thereof.

16. The method of claim 1, wherein the downstream adaptor comprises a nick translation initiation site.

17. The method of claim 16, wherein said downstream adaptor further comprises a hybridization domain, a ligation domain, a detection domain, an amplification domain, a recombination domain, or a combination thereof.

18. The method of claim 1, wherein the upstream adaptor comprises at least a first and second upstream adaptor molecule construct.

19. The method of claim 1, wherein the upstream adaptor comprises a plurality of upstream adaptor molecule constructs.

20. The method of claim 18, wherein said at least a first and second upstream adaptor molecule constructs have different primer binding regions.

21. The method of claim 1, wherein the downstream adaptor comprises at least a first and second downstream adaptor molecule construct.

22. The method of claim 1, wherein the downstream adaptor comprises a plurality of downstream adaptor molecule constructs.

23. The method of claim 21, wherein the at least a first and second downstream adaptor molecule constructs have different primer binding regions.

24. The method of claim 1, further comprising amplifying adaptor attached DNA molecules.

25. The method of claim 24, wherein the amplified DNA is cloned into a vector.

26. The method of claim 24, wherein the amplified DNA is sequenced.

27. The method of claim 24, wherein the amplified DNA is separated.

28. The method of claim 1 or 24, further comprising creating a DNA library.

29. The method of claim 28, wherein the DNA library is an unordered DNA library.

30. The method of claim 28, wherein the DNA library is an ordered DNA library.

31. The method of claim 30, wherein creation of the ordered DNA library further comprises recombination.

32. The method of claim 30, wherein the ordered DNA library comprises a plurality of nick translate molecules wherein nick translation of said nick translate molecules is carried out for different periods of time.

33. The method of claim 30, wherein the ordered DNA library is further defined as a genomic ordered positional library.

34. The method of claim 24, wherein the adaptor attached nick translate molecules are amplified with primers complementary to the upstream adaptor molecule and the downstream adaptor molecule.

35. The method of claim 24, wherein the adaptor attached nick translate molecules are amplified with a first primer specific to the upstream adaptor and a second primer specific to an internal sequence of the nick translate molecule.

36. The method of claim 24, wherein the adaptor attached nick translate molecules are amplified with a first primer specific to the downstream adaptor molecule and a second primer specific to an internal sequence of the nick translate molecule.

37. The method of claim 24, wherein at least one of the primers used for amplification of the adaptor attached nick translate molecules is labeled.

38. A method of creating hybridization probes comprising preparing a labeled, amplified DNA in accordance with the method of claim 37.

39. The method of claim 1, further comprising subjecting the adaptor attached nick translate molecules to recombination.

40. The method of claim 1, wherein said downstream adaptor is attached at said nick site.

41. The method of claim 40, wherein said attachment is to the 5′ strand of said nick site.

42. The method of claim 40, wherein said attachment is to the 3′ strand of said nick site.

43. The method of claim 39, wherein said recombination occurs at low DNA concentrations.

44. The method of claim 39, wherein said recombination comprises:

a) digesting the DNA molecule with a first sequence-specific endonuclease;

b) ligating both strands of an adaptor molecule to the sequence-specific termini of the template molecules;

c) digesting the DNA molecules with a second sequence-specific endonuclease;

d) incubating the DNA molecules at low concentration with large amount of T4 DNA ligase;

e) concentrating the DNA molecules;

f) initiating a nick-translation reaction for a controlled time; and

g) attaching a down-stream adaptor.

45. The method of claim 39, wherein said recombination comprises:

a) methylating the DNA molecules;

b) ligating a first and second adaptor to the ends of the DNA molecule to form a recognition sequence, a single nick-translation initiation site, and a single Eco RI restriction recognition sequence within the recombination domain;

c) activating the adaptors by incubation with a restriction enzyme or nuclease;

d) incubating the DNA molecules at low concentration with a large amount of T4 DNA ligase;

e) concentrating the DNA molecules;

f) initiating a nick-translation reaction for a controlled time; and

g) attaching a down-stream adaptor.

46. The method of claim 1, wherein the adaptor attached nick translate molecules are between .5 and 500 kB in length.

47. The method of claim 1, wherein the DNA sample is cDNA.

48. The method of claim 1, wherein the DNA sample is genomic DNA.

49. The method of claim 1, wherein the DNA sample is cloned DNA.

50. The method of claim 1, wherein the DNA sample is a BAC.

51. The method of claim 1, wherein the DNA sample is a YAC.

52. The method of claim 1, wherein the DNA sample is a cosmid.

53. The method of claim 1, wherein the DNA sample is a large insert clone.

54. A method of shotgun sequencing of DNA comprising the steps of:

a) preparing a DNA library in accordance with claim 30;

b) sequencing the library using primers specific for known loci to derive the sequence of adjacent unknown regions.

55. The method of claim 1, further comprising:

a) recombining the DNA molecules after adaptor attachment;

b) size separating the DNA molecules;

c) amplifying the DNA.

56. The method of claim 55, wherein the size separated DNA is distributed into the wells of a multi-well plate.

57. The method of claim 55, wherein the amplified DNA is sequenced.

58. The method of claim 55, wherein the amplified DNA is subsequently cloned into a vector.

59. The method of claim 1, further comprising:

a) amplifying the DNA molecules after adaptor attachment;

b) hybridizing the amplified DNA to a microarray;

c) analyzing the hybridization patterns.

60. The method of claim 1, wherein the DNA sample is modified.

61. The method of claim 60, wherein the DNA sample is methylated.

62. The method of claim 1, further comprising:

a) initiating a second nick translation reaction at the upstream adaptor comprising subjecting the DNA molecules to nick translation using a DNA polymerase having 5′-3′ exonuclease activity;

b) attaching second downstream adaptor molecules to the 5′ end of the molecules to produce adaptor attached nick translate molecules.

63. The method of claim 1, further comprising:

a) denaturing the adaptor attached nick translation product and separating the single stranded DNA;

b) replicating the second strand of the adaptor attached molecule to form a double stranded product;

c) subjecting the DNA molecules to nick translation using a DNA polymerase having 5′-3′ exonuclease activity, to produce nick translate molecules;

d) attaching additional downstream adaptor molecules to the nick translation initiation site of the nick translate molecules to produce adaptor attached nick translate molecule molecules

64. The method of claim 1, wherein an affinity adaptor is ligated to said DNA molecules.

65. The method of claim 64, wherein said affinity adaptor is used to separate DNA molecules.

66. The method of claim 3, wherein said restriction digestion is carried out with a frequent cutter.

67. The method of claim 3, wherein said restriction digestion is carried out with an infrequent cutter.

68. The method of claim 3, wherein said restriction digestion results in partial cleavage.

69. The method of claim 1, further comprising attaching the upstream adaptor molecule to both the proximal and distal ends of said DNA molecules to create a circular product.

70. The method of claim 69, wherein the initiation of nick translation occurs in the direction of the distal end of the nick translate molecule subjected to circularization.

71. The method of claim 69, wherein different internal regions of the nick translate molecules are exposed as distal ends.

72. The method of claim 19, wherein nick translation is carried out on a DNA sample with a plurality of upstream adaptors in a single tube.

73. The method of claim 22, wherein nick translation is carried out on a DNA sample with a plurality of downstream adaptors, in a single tube

74. The method of claim 1, wherein the nick translation reaction proceeds through a known sequence on the DNA molecule.

75. The method of claim 74, wherein PCR primers are constructed to recognize regions within said known sequence.

76. The method of claim 75, wherein PCR amplification of nick translate products occurs using a primers specific to said known sequence and a primers specific to an attached adaptor.

77. The method of claim 1, further comprising circularizing the adaptor attached, nick translate product by:

a) incubating said adaptor attached, nick translate product with a linker oligonucleotide to form a nick site; and

b) ligating the ends of said adaptor attached, nick translate product with a DNA ligase.

78. The method of claim 77, wherein said linker oligonucleotide is 20-200 bp. long.

79. The method of claim 77, wherein said linker oligonucleotide has a region complementary to the upstream adaptor and a region complementary to the downstream adaptor.

80. The method of claim 1, wherein:

a) the DNA molecules of the DNA sample are restricted with one or more restriction enzymes;

b) upstream adaptor molecules are attached at both ends of the restricted DNA molecules;

c) nick translation is carried out from both upstream adaptors; and

d) the ends of the DNA molecules are recombined.

81. The method of claim 80, further comprising separating the recombined molecules according to size.

82. The method of claim 80, wherein said restriction enzyme is a frequent cutter.

83. The method of claim 82, wherein said restriction digestion is a partial digest.

84. The method of claim 80, wherein the each end of the DNA molecule is created with a different restriction enzyme.

85. The method of claim 1, wherein:

a) the DNA molecules of the DNA sample are restricted with an infrequent cutting restriction enzyme;

b) upstream adaptor molecules are attached at ends of the restricted DNA molecules;

c) nick translation is carried out from the upstream adaptors;

d) the nick translate molecules are partially restricted with a frequent cutter;

e) internal adaptor molecules are attached at ends of the restricted DNA molecules;

f) nick translation is carried out from the internal adaptors; and

g) the ends of the DNA molecules are recombined.

86. The method of claim 1, wherein nucleotides integrated by nick translation are modified.

87. The method of claim 86, wherein the modified nucleotides are exonuclease resistant.

88. The method of claim 87, wherein said modified nucleotides facilitates the differentiation of the nick translate product from the template strand.

89. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching upstream adaptor molecules to the proximal end of DNA molecules of the sample to provide a nick translation initiation site;

c) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T;

d) attaching downstream adaptor molecules to the 5′ end of the degraded template strand to produce adaptor attached nick translate molecules.

90. The method of claim 89, wherein said adaptor attached nick translate molecules are amplified.

91. The method of claim 89, wherein a plurality of DNA molecules from said DNA sample are reacted for a different time T.

92. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching upstream adaptor molecules to the proximal end of DNA molecules of the sample to provide a nick translation initiation site;

c) subjecting the DNA molecules to a first nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T;

d) attaching first downstream adaptor molecules to the 3′ end of the nick translate product to produce adaptor attached nick translate molecules.

e) subjecting the DNA molecules to a second nick translation initiated from the upstream adaptor comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T; and

f) attaching second downstream adaptor molecules to the 5′ end of the degraded nick translate product.

93. The method of claim 92, wherein said adaptor attached nick translate molecules are amplified.

94. The method of claim 92, wherein a plurality of DNA molecules from said DNA sample are subjected to nick translation for a first time for a different time T.

95. The method of claim 92, wherein a plurality of DNA molecules from said DNA sample are subjected to nick translation for a second time for a different time T.

96. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching upstream adaptor molecules to the proximal end of DNA molecules of the sample to provide a nick translation initiation site;

c) subjecting the DNA molecules to a first nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T;

d) attaching a first downstream adaptor molecules to the 3′ end of the nick translate product;

e) separating the nick translate product from the template molecule;

f) replicating the nick translate product via primer extension;

g) subjecting the product of step f) to a second nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T; and

h) attaching a second downstream adaptor molecules to the 3′ end of the product of step g).

97. The method of claim 96, wherein said adaptor attached nick translate molecules are amplified.

98. The method of claim 96, wherein a plurality of DNA molecules from said DNA sample are subjected to nick translation for a first time for a different time T..

99. The method of claim 96, wherein a plurality of DNA molecules from said DNA sample are subjected to nick translation for a second time for a different time T..

100. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) ligating an affinity adaptor to the proximal ends of said DNA molecules;

c) subjecting the affinity adaptor attached molecules to partial cleavage;

d) separating the affinity adaptor attached molecules;

e) attaching upstream adaptor molecules to ends of the affinity adaptor attached molecules to provide a nick translation initiation site;

f) subjecting the affinity adaptor attached molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity; and

g) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

101. The method of claim 100, wherein said adaptor attached nick translate molecules are amplified.

102. The method of claim 100, wherein said polymerization incorporates modified nucleotides.

103. The method of claim 102, wherein incorporation of said modified nucleotides are exonuclease resistant.

104. The method of claim 100, wherein said adaptor attached nick translate molecules are separated.

105. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching the first end of a recombination adaptor to one end of said DNA molecules;

c) attaching the second end of said recombination adaptor to the opposite end of said DNA molecules;

d) subjecting the adaptor attached molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity; and

e) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

106. The method of claim 105, wherein said adaptor attached nick translate molecules are amplified.

107. The method of claim 105, wherein said adaptor attached nick translate molecules are separated.

108. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching the first end of a recombination adaptor to the proximal end of said DNA molecules;

c) partially cleaving said DNA molecules to produce cleavage products having a plurality of lengths;

d) attaching the second end of said recombination adaptor to distal ends produced by said partial cleavage;

e) subjecting the adaptor attached molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity;

f) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules; and

g) separating said adaptor attached nick translate molecules.

109. The method of claim 108, wherein said partial cleavage is performed with a restriction enzyme.

110. The method of claim 108, wherein said partial cleavage is performed with an endonuclease.

111. The method of claim 108, wherein said partial cleavage is performed by chemical cleavage.

112. The method of claim 108, wherein said adaptor attached nick translate molecules are amplified.

113. The method of claim 108, wherein said separation is based upon size.

114. A method of preparing DNA molecules having an amplifiable region comprising:

a) obtaining a first DNA template;

b) attaching a first upstream adaptor molecules to said DNA template to provide a nick translation initiation site;

c) obtaining a second DNA template;

d) attaching a second upstream adaptor molecules to said DNA template to provide a nick translation initiation site;

e) mixing said first and said second templates;

f) subjecting the adaptor attached template molecules to nick translation initiated from the upstream adaptor comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T; and

g) attaching a downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

115. The method of claim 114, wherein said adaptor attached nick translate molecules are amplified.

116. The method of claim 114, wherein said adaptor attached molecules are subsequently differentiated by PCR amplification employing primers specific for said first upstream adaptor and/or said second upstream adaptor.

117. A method of preparing DNA molecules having an amplifiable region comprising:

a) obtaining a plurality of DNA templates;

b) attaching a plurality of different first upstream adaptor molecules to said DNA templates to provide a nick translation initiation site;

c) mixing said plurality of templates;

d) subjecting the adaptor attached template molecules to nick translation initiated from the upstream adaptor comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T; and

e) attaching a downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

118. The method of claim 117, wherein said adaptor attached nick translate molecules are amplified.

119. The method of claim 117, wherein said adaptor attached molecules are subsequently differentiated by PCR amplification employing primers specific for said first upstream adaptor or said second upstream adaptor.

120. A method of constructing a genomic library, comprising:

a) obtaining genomic DNA;

b) fragmenting the genome to a desired size;

c) attaching upstream adaptor molecules to ends of the fragmented genomic DNA molecules of the sample to provide a nick translation initiation site;

d) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity; and

e) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

121. The method of claim 120, wherein said adaptor attached nick translate molecules are amplified.

122. The method of claim 120, wherein said nick translate molecules contain a known, kernel sequence.

123. The method of claim 120, wherein said nick translate molecules are amplified with a primer or primers specific for said kernel sequence.

124. The method of claim 120, wherein said nick translate molecules are recombined.

125. The method of claim 124, wherein said recombination comprises ligating said upstream adaptor to said downstream adaptor.

126. The method of claim 124, wherein said recombined molecule further comprises a kernel sequence.

127. The method of claim 124, wherein sequences adjacent to said kernel sequence are amplified.

128. The method of claim 120, wherein said adaptor attached nick translate molecules are inserted into a vector.

129. The method of claim 120, wherein said adaptor attached nick translate molecules are sequenced.

130. The method of claim 120, wherein said adaptor attached nick translate molecules are separated.

131. The method of claim 130, wherein said separation is based upon size.

132. The method of claim 120, wherein said upstream adaptor comprises a free 5′ phosphate group.

133. The method of claim 120, wherein said adaptor attached nick translate molecule is recombined with a DNA ligase employing a linking oligonucleotide.

134. The method of claim 133, further comprising:

a) incubating said linking oligonucleotide with said adaptor attached nick; and translate molecule to form a nick

b) ligating the adaptor attached nick translate molecule with a DNA ligase.

135. The method of claim 134, wherein said ligase is thermostable.

136. The method of claim 134, wherein said recombination is performed at a low DNA concentration.

137. A method of constructing a genomic library, comprising:

a) obtaining a genomic DNA;

b) fragmenting the genomic DNA;

c) attaching upstream adaptor molecules to ends of the fragmented genomic DNA molecules of the sample to provide a nick translation initiation site;

d) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, for a specific time T; and

e) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

138. The method of claim 138, further comprising the step of subdividing the upstream-adaptor attached genomic DNA molecules into a plurality of reaction vessels.

139. The method of claim 137, wherein said adaptor attached nick translate molecules are amplified.

140. The method of claim 137, wherein said nick translate molecules contain a known, kernel sequence.

141. The method of claim 137, wherein said nick translate molecules are amplified with a primer or primers specific for said kernel sequence.

142. The method of claim 137, wherein said nick translate molecules are recombined.

143. The method of claim 142, wherein said recombination comprises ligating said upstream adaptor to said downstream adaptor.

144. The method of claim 142, wherein said recombined molecule further comprises a kernel sequence.

145. The method of claim 144, wherein sequences adjacent to said kernel sequence are amplified.

146. The method of claim 138, wherein said adaptor attached nick translate molecules are inserted into a vector.

147. The method of claim 138, wherein said adaptor attached nick translate molecules are sequenced.

148. The method of claim 138, wherein said adaptor attached nick translate molecules are separated.

149. The method of claim 148, wherein said separation is based upon size.

150. The method of claim 138, wherein said upstream adaptor comprises a 5′ phosphate group.

151. The method of claim 138, wherein said adaptor attached nick translate molecule is recombined with a DNA ligase employing a linking oligonucleotide.

152. The method of claim 151, further comprising:

a) incubating said linking oligonucleotide with said adaptor attached nick translate molecule to form a nick; and

b) ligating the adaptor attached nick translate molecule to the linking oligonucleotide with a DNA ligase.

153. The method of claim 152, wherein said ligase is thermostable.

154. The method of claim 152, wherein said recombination is performed at a low nick translate molecule concentration.

155. The method of claim 138, wherein the specific time T varies for different reaction vessels.

156. A method of preparing an unordered DNA library comprising:

a) obtaining a DNA sample comprising DNA molecules;

b) cleaving said DNA molecules;

c) attaching recombination adaptors to termini of the cleaved DNA molecules;

d) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, to produce nick translate molecules wherein said nick translation is initiated from both ends of the cleaved DNA molecules; and

e) recombining the ends of the nick translate molecules produced by step d).

157. The method of claim 156, wherein said recombined molecules are amplified

158. The method of claim 156, wherein said recombined molecules are sequenced.

159. The method of claim 156, wherein said recombined molecules are separated.

160. The method of claim 159, wherein said separation is based upon size.

161. A method of producing an ordered DNA library comprising:

a) obtaining a DNA sample comprising DNA molecules;

b) cleaving said DNA molecules;

c) partially cleaving the cleaved DNA molecules;

d) attaching adaptors to termini of the DNA molecules;

e) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity, to produce nick translate molecules wherein said nick translation is initiated from both ends of the DNA molecules;

f) separating the nick translate molecules; and

g) subjecting the separated nick translate molecules to recombination.

162. A method of producing an ordered library comprising:

a) obtaining a DNA sample comprising DNA molecules;

b) cleaving said DNA molecules;

c) attaching recombination adaptors to termini of the DNA molecules;

d) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5'-3' exonuclease activity, to produce nick translate molecules wherein said nick translation is initiated from both ends of the DNA molecules;

e) recombining the ends of the DNA molecules produced by step d);

f) separating the nick translate molecules according to size.

163. The method of claim 161, wherein said recombined nick translate molecules are amplified.

164. The method of claim 163, wherein nucleotide analogs are integrated during said amplification.

165. The method of claim 161, wherein said recombined nick translate molecules contain a known sequence.

166. The method of claim 163, wherein said recombined nick translate molecules are amplified with at least one primer specific for sequence within said known sequence.

167. The method of claim 166, wherein the time of primer extension is limited.

168. The method of claim 166, wherein the amplified recombined nick translate molecules are subsequently separated.

169. The method of claim 161, wherein said adaptors are covalently joined by recombination.

170. The method of claim 163, wherein said amplified recombined nick translate molecules are sequenced.

171. The method of claim 163, wherein said recombined nick translate molecules are diluted prior to amplification.

172. The method of claim 171, wherein said dilution results in a reaction mixture with only a single DNA molecule.

173. The method of claim 170, wherein said sequencing is cycle sequencing.

174. The method of claim 172, wherein said cycle sequencing employs a primer complementary to an adaptor and at least one or two base pairs adjacent to said adaptor.

175. The method of claim 170, wherein said amplified recombined nick translate molecules are cloned into a vector prior to sequencing.

176. A method of creating a DNA library, comprising:

a) obtaining a DNA sample comprising DNA molecules;

b) cleaving said DNA molecules with an infrequently-cutting restriction enzyme;

c) attaching upstream adaptor molecules to ends of said cleaved DNA molecules of the sample to provide a nick translation initiation site;

d) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity;

e) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

f) partially cleaving the adaptor attached nick translate molecules with a frequently cutting restriction enzyme;

g) attaching upstream adaptor molecules to the ends of the adaptor attached nick translate molecules produced by said partial digestion;

h) subjecting the DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity; and

i) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules;

j) subjecting the product of step i) to recombination.

177. The method of claim 176, wherein said recombined molecules are separated.

178. The method of claim 176, wherein said recombined molecules are amplified.

179. The method of claim 178, wherein said amplification comprises at least one primer specific for an adaptor.

180. The method of claim 178, wherein said recombined molecules contain a known, kernel sequence.

181. The method of claim 180, wherein said amplification comprises at least one primer specific for said known, kernel sequence.

182. The method of claim 39, wherein said upstream and downstream adaptors further comprise long 3′ tails.

183. The method of claim 39, wherein said upstream and downstream adaptors comprise a nick site that facilitates nick translation through the intermolecular junction.

184. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) ligating at least a first upstream adaptor and at least a second upstream adaptor to said DNA molecules;

c) subjecting the DNA molecules to recombination at low DNA concentrations;

d) subjecting the recombined DNA molecules to nick translation comprising DNA polymerization and 5′-3′ exonuclease activity; and

e) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

185. The method of claim 184, wherein said adaptor attached nick translate molecules are subsequently sequenced.

186. The method of claim 1, wherein said DNA sample comprises short template molecules of 1-20 kb.

187. A method of sequencing a BAC clone, comprising:

a) cleaving the BAC clone at a *cos* site with lambda terminase

b) ligating an upstream adaptor to the 5′ overhangs;

c) partially cleaving the BAC clone with a frequently cutting enzyme;

d) recombining the partially cleaved BAC clone of step c);

e) adding a homopolymeric tail to the 3′ end of the recombined product with terminal transferase;

f) ligating an adaptor having a homopolymeric 3′ single-strand overhang and a unique double strand sequence at the end to the homopolymeric tail, wherein the homopolymeric single-strand overhang is complementary to the homopolymeric tail of step e);

g) size separating the product of step f);

h) distributing the separated product into the wells of a microplate.

i) amplifying the separated products with primers complementary to adaptor sequences such that products are formed which proceed in either a clockwise or counterclockwise direction around the recombined molecule;

j) ligating the amplified product into a cloning vector; and

k) subsequently sequencing said amplified product.

188. The method of claim 1, wherein said adaptor attached nick translate molecules are distributed as an ordered microarray.

189. The method of claim 188, wherein said microarray is probed with complementary nucleic acid.

190. A kit comprising amplifiable DNA, wherein said DNA is prepared by the method of claim 1.

191. The kit of claim 190, wherein said DNA is genomic DNA.

192. The kit of claim 191, wherein said genomic DNA is isolated from a prokaryotic.

193. The kit of claim 191, wherein said genomic DNA is isolated from a eukaryotic.

194. The kit of claim 191, wherein said genomic DNA is isolated from an animal.

195. The kit of claim 194, wherein said animal is selected from the group consisting of human, feline, canine, bovine, equine, porcine, caprine, murine, lupine, ranine, piscine and simian

196. The kit of claim 191, wherein said genomic DNA is isolated from a plant.

197. The kit of claim 196, wherein said plant is a dicotyledonous plant.

198. The kit of claim 197, wherein said dicotyledonous plant is selected from the group consisting of tobacco, tomato, potato, sugar beet, pea, carrot, cauliflower, broccoli, soybean, canola, sunflower, alfalfa, cotton and *Arabidopsis*.

199. The kit of claim 195, wherein said DNA is isolated from a monocotyledonous plant.

200. The kit of claim 199, wherein said monocotyledonous plant is selected from the group consisting of wheat, maize, rye, rice, turfgrass, oat, barley, sorghum, millet, and sugarcane.

201. An adaptor construct, wherein said construct comprises:

a) a first domain comprising nucleotides that facilitate ligation of said construct to a nucleic acid; and

b) a second domain proximal to said first domain, comprising a site which facilitates the initiation of a nick translation reaction and a site that facilitates recombination.

wherein ligation of said adaptor construct to a polynucleotide molecule results in the only free 3′ OH group capable of initiating a nick translation reaction within said second domain.

202. The adaptor construct of claim 201, further comprising a primer binding site, a hybridization domain, a detection domain, an amplification domain, a recombination domain, or a combination thereof.

203. The adaptor construct of claim 201, wherein said first domain comprises a nucleotide overhang.

204. The adaptor construct of claim 201, wherein said site for initiation of a nick translation reaction comprises a single stranded region in an otherwise essentially double stranded molecule.

205. The adaptor construct of claim 201, wherein said adaptor construct further comprises a domain that inhibits self ligation of said adaptor.

206. The adaptor construct of claim 201, wherein said construct further comprises at least one degradable base.

207. The adaptor construct of claim 206, wherein said at least one degradable base is degraded in order to create said free 3′ OH group.

208. The adaptor construct of claim 207, wherein said at least one degradable base is deoxyribouracil.

209. An adaptor construct comprising:

a) a first oligonucleotide comprising a phosphate group at the 5′ end and a blocking nucleotide at the 3′ end;

b) a second oligonucleotide comprising a blocked 3′ end, a non-phosphorylated 5′ end, and a nucleotide sequence complementary to the 5′ element of said first oligonucleotide ; and

c) a third oligonucleotide comprising a 3′ hydroxyl group, a non-phosphorylated 5′ end, and a nucleotide sequence complementary to the 3′ element of said first oligonucleotide.

210. The adaptor construct of claim 209, wherein said first oligonucleotide is from about 10 to about 200 bases.

211. The adaptor construct of claim 209, wherein said second and said third oligonucleotide are from about 5 to about 195 bases.

212. The adaptor construct of claim 209, wherein said first oligonucleotide further comprises an additional 3′ tail.

213. The adaptor construct of claim 209, wherein said first oligonucleotide comprises a 3′ end protected from exonuclease activity.

214. The adaptor construct of claim 209 wherein said first oligonucleotide comprises one or more nuclease resistant nucleotide analogs.

215. The adaptor construct of claim 209, wherein said third oligonucleotide comprises a 3′ end capable of initiating a nick translation reaction.

216. An adaptor construct comprising

a) a first oligonucleotide comprising a 5′ phosphate and a 3′ nucleotide blocked to prevent ligation or extension by a polymerase;

b) a second oligonucleotide comprising a domain which facilitates ligation to the template strand and a nucleotide sequence complementary to the 5′ element of said first oligonucleotide;

c) a third oligonucleotide comprising an initiation site for nick-translation and a nucleotide sequence complementary to a region of said first oligonucleotide; and

d) a plurality of oligonucleotides which may be readily removed to expose a 3′ terminus of the adaptor, wherein each of said plurality of oligonucleotides comprise a nucleotide sequence complementary to a region of said first oligonucleotide.

217. The adaptor construct of claim 216, wherein removal of said plurality of oligonucleotides creates a site that facilitates recombination.

218. An adaptor construct, wherein said construct comprises:

a) a first domain comprising nucleotides that facilitate ligation of said construct to a nucleic acid; and

b) a second domain proximal to said first domain, comprising a site which facilitates the initiation of a nick translation reaction,

c) a third domain proximal to said first domain, comprising a second site which facilitates the initiation of a nick translation reaction, said second or said third domain further comprising a site that facilitates recombination, wherein ligation of said adaptor construct to a polynucleotide molecule results in the only free 3′ OH groups capable of initiating a nick translation reaction within said second and said third domains.

219. The adaptor construct of claim 218, further comprising a primer binding site.

220. The adaptor construct of claim 218, wherein said first domain comprises a nucleotide overhang.

221. The adaptor construct of claim 218, wherein said site for initiation of a nick translation reaction comprises a single stranded region in an otherwise essentially double stranded molecule.

222. The adaptor construct of claim 218, wherein said adaptor construct further comprises a domain that inhibits self ligation of said adaptor.

223. The adaptor constructive claim 218, wherein said adaptor construct comprises a single ligatable terminus.

224. The adaptor construct of claim 218, wherein said adaptor construct is ligated to a nucleic acid molecule and wherein following said ligation there is only a single free 3′ OH group capable of initiating a nick translation reaction.

225. The adaptor construct of claim 218, wherein said adaptor construct comprises one or more nuclease resistant nucleotide analogs.

226. An adaptor construct comprising:

a) a first oligonucleotide comprising a phosphate group at the 5′ end and a blocking nucleotide at the 3′ end;

b) a second oligonucleotide comprising a blocked 3′ end, a non-phosphorylated 5′ end, and a nucleotide sequence complementary to the 5′ element of said first oligonucleotide ;

c) a third oligonucleotide comprising a 3′ hydroxyl group, a non-phosphorylated 5′ end, and a nucleotide sequence complementary to the 3′ element of said first oligonucleotide; and

d) a fourth oligonucleotide comprising a 3′ hydroxyl group, a non-phosphorylated 5′ end, and a nucleotide sequence complementary to the 3′ element of said first oligonucleotide.

227. The adaptor construct of claim 226 wherein said first oligonucleotide is from about 10 to about 200 bases.

228. The adaptor construct of claim 226, wherein said second, said third and said fourth oligonucleotides are from about 5 to about 195 bases.

229. The adaptor construct of claim 226, wherein said first oligonucleotide further comprises an additional 3′ tail.

230. The adaptor construct of claim 226, wherein said first oligonucleotide comprises a 3′ end protected from exonuclease activity.

231. The adaptor construct of claim 226, wherein said first oligonucleotide comprises one or more nuclease resistant nucleotide analogs.

232. The adaptor construct of claim 226, wherein said third oligonucleotide comprises a 3′ end capable of initiating a nick translation reaction.

233. An adaptor construct comprising:

a) a first oligonucleotide comprising a 5′ region comprising a 5′ phosphate group and homopolymeric tract of about 8-20 bases and a 3′ region comprising an about 12- about 100 base primer binding domain; and

b) a second oligonucleotide complementary to the 3′ region of said first oligonucleotide.

234. The adaptor construct of claim 233, further comprising a recombination site.

235. An adaptor construct comprising:

a) a first oligonucleotide of about 12- about 100 bases, wherein the 5′ end of said oligonucleotide comprises a free phosphate group; and

b) a second oligonucleotide comprising a homopolymeric tract of about 8 – 20 bases, a 3′ blocking nucleotide and wherein the 5′ region of said second oligonucleotide is complementary to said first oligonucleotide.

236. The adaptor construct of claim 235, further comprising a recombination site.

237. An adaptor construct comprising:

a) a first oligonucleotide comprising a 5′ region comprising an about 12- about 100 base primer binding domain and a 3′ region comprising a homopolymeric tract of about 8- about 20 bases; and

b) a second oligonucleotide comprising a blocked 3′ end and a 3′ region complementary to the 5′ region of said first oligonucleotide.

238. The adaptor construct of claim 237, further comprising a recombination site.

239. An adaptor construct comprising:

a) a first oligonucleotide comprising a 5′ region comprising an about 12- about 100 base primer binding domain; and

b) a second oligonucleotide a homopolymeric tract of about 4 – about 12 bases at the 5′ end, a blocking nucleotide at the 3′ end, and a 3′ region complementary to said first oligonucleotide.

240. The adaptor construct of claim 239, further comprising a recombination site.

241. A method of preparing a DNA molecule having an amplifiable region comprising:

a) obtaining a DNA sample comprising DNA molecules having regions to be amplified;

b) attaching upstream adaptor molecules to ends of DNA molecules of the sample to provide a nick translation initiation site;

c) subjecting the DNA molecules to nick translation comprising DNA polymerization, to produce nick translate molecules; and

d) attaching downstream adaptor molecules to the nick translate molecules to produce adaptor attached nick translate molecules.

242. The method of claim 241, wherein said adaptor attached nick translate molecules are amplified.

243. The method of claim 241, wherein said adaptor attached nick translate molecules are sequenced.

244. The method of claim 241, wherein said adaptor attached nick translate molecules are cloned into a vector.

245. The method of claim 241, wherein said adaptor attached nick translate molecules are recombined

246. The method of claim 241, wherein said adaptor attached nick translate molecules are separated

247. The method of claim 241, wherein said adaptor attached nick translate molecules comprise a DNA library.

248. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 201.

249. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 209.

250. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 216.

251. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 218.

252. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 226.

253. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 233.

254. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 235.

255. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 237.

256. A kit, wherein said kit comprises:

a) a DNA polymerase;

b) nucleotide triphosphates; and

c) the adaptor construct of claim 239.

257. The method of claim 1, wherein said adaptor attached nick translate molecules are assembled as a microarray, and wherein said nick translate molecules are amplified prior to said assembly.

258. The microarray of claim 257, wherein said microarray is assembled on a DNA chip.

259. The DNA chip of claim 258, wherein said DNA chip comprises an array of adaptor attached nick translate molecules that facilitate analysis of a patient sample to determine chromosomal mutations.

260. The DNA chip of claim 258, wherein said DNA chip comprises an array of adaptor attached nick translate molecules that facilitate diagnostic mutation analysis.

261. A method of recombining DNA molecules comprising recombining ends of adaptor attached template molecules in a dilute solution.

262. The method of claim 261, wherein said recombination is further characterized as:

a) cleaving said DNA molecules with a first sequence-specific endonuclease;

b) ligating an adaptor to the sequence-specific termini of the DNA molecule;

c) cleaving said DNA molecules with a second sequence-specific endonuclease;

d) incubating the DNA molecules under conditions to promote intramolecule ligation of the DNA molecules; and

e) concentrating said DNA molecules.

263. The method of claim 262, wherein said second sequence-specific endonuclease partially cleaves said DNA molecules.

264. The method of claim 261, wherein said recombination is further characterized as:

a) methylating said DNA molecules;

b) attaching a first and second adaptor to the ends of said DNA molecules, wherein said adaptors comprise an activatable region;

c) activating said adaptors by incubation with a restriction endonuclease thereby removing distal portion of the adaptors and creating sticky ends;

d) incubating the DNA molecules under conditions to promote intramolecule ligation of the DNA molecules; and

e) concentrating said DNA molecules.

265. A method of recombining DNA molecules comprising:

a) hybridizing the ends of adaptor attached template molecules in dilute solution;

b) concentrating the molecules; and

c) ligating the molecules.

266. A method of recombining DNA molecules comprising:

a) hybridizing the ends of adaptor attached template molecules; and

b) subjecting said molecule to a nick-translation reaction to form a covalent intramolecular junction.

267. A method of detecting a specific DNA sequence, comprising:

a) separating adaptor attached nick translate molecules; and

b) identifying said DNA sequence.

268. The method of claim 267, further comprising:

a) hybridizing said adaptor attached nick translate molecules to a DNA microarray; and

b) detecting said hybridization.

269. The method of claim 267, wherein a plurality of specific DNA sequences are detected.

270. The method of claim 267, wherein the adaptor attached nick translate molecules are from a human individual.

271. The method of claim 267, wherein the adaptor attached nick translate molecules are from a plurality of human individuals.

272. The method of claim 267, wherein the adaptor attached nick translate molecules are from a plurality of microorganisms.